Remarks

The present application is directed to a method for detecting the presence of a target nucleic acid sequence in a sample by amplifying the target to produce an amplification reaction product that includes a purine rich region, contacting the sample with a peptide nucleic acid able to bind to at least a portion of the target sequence and detecting the presence of triplex DNA structures. The application is also directed to a kit containing a peptide nucleic acid (PNA) sequence designed to form a triplex with a target sequence and a set of amplification primers that can amplify a sequence including the target sequence.

Claims 14 and 16 have been cancelled without prejudice. New Claims 25 and 26 have added. Support for these new claims can be found at least in the original description at page 5, lines 12-17, and in canceled Claims 14 and 16. Upon entry of the amendment, Claims 1-2, 5-6, 8-12, and 18-26 will be pending.

Rejection Under 35 U.S.C. 103(a)

In the Office Action mailed November 15, 2005, the Examiner rejected Claims 1, 5-6, 8-12, 14, 16 and 18-24 under 35 U.S.C. § 103(a) as being obvious over Vary (U.S. Patent No. 5,800,984) in view of Kai *et al.* (*Nucleic Acids Symposium Series* No. 37:321-322, 1997). Applicants respectfully traverse.

Vary discloses DNA triplex formation as a means of detecting a nucleic acid target sequence, for example a PCR product. Applicants respectfully submit that Vary fails to disclose the use of **PNA** probes for forming and detecting such a triplex.

Kai *et al.* describes the use of a PNA probe designed to hybridize with a gene encoding Verotoxin 2. The PNA probe is immobilized on the surface of a sensor chip of a BIAcore surface plasmon resonance system. As explained in the paragraph bridging columns 1 and 2 on page 321 of Kai *et al.*, PNA forms stable duplexes with single stranded DNA

under conditions in which DNA duplexes are unstable, such as low salt concentrations. The method of Kai *et al.* involves generating a (double-stranded DNA) PCR product, and then subjecting the PCR product to denaturing conditions in the presence of 10% formamide. The denaturing conditions make the double-stranded DNA unstable and result in the formation of single-stranded DNA, which then anneals preferentially to the immobilized PNA probe to form a PNA/DNA duplex (see final paragraph, column 2, page 321).

The method of Kai *et al.* is described in more detail in a subsequent paper by the same group, i.e. Sawata *et al.* and is enclosed for the Examiner's convenience. It is clear from Sawata *et al.* that the denaturing conditions, which include 10% formamide as described in Kai *et al.*, preferentially results in the formation of **PNA/DNA** duplexes rather than **DNA/DNA** duplexes.

Therefore, contrary to the assertions of the Examiner, Kai *et al.* fails to disclose formation and detection of a **triplex** structure containing PNA and double-stranded DNA. Furthermore, the method of Kai *et al.* is not a **real-time** PCR reaction because the PCR reaction products must be subjected at end-point (after 20 cycles – see final paragraph, column 2, page 321) to the above-described denaturing conditions so that one of the strands of the double-stranded DNA PCR product can be displaced to form the PNA/DNA **duplex**.

Applicants respectfully submit that, for a rejection under 35 U.S.C. § 103 to be properly founded, each and every element of the claim must be disclosed in the combination of cited art references. Vary and Kai *et al.* individually or combined **fail** to disclose the use of PNA to detect triplex structures resulting from the binding of amplified target sequence to PNA, as required in the presently claimed method and kit. One of ordinary skill in the art would therefore lack the motivation to make or use the claimed method or kit in view of the disclosures by Kai *et al.* and Vary. For at least the foregoing reasons, withdrawal of the rejection is respectfully requested.

The Examiner rejected Claim 2 under 35 U.S.C. § 103(a) as being unpatentable over Vary in view of Kai *et al.* and further in view of Armitage *et al.* (1997).

Claim 2 specifies that the peptide nucleic acid is bis-PNA.

As stated above, Vary and Kai *et al.* individually or combined fail to disclose or teach the method recited in Claim 1, on which Claim 2 is dependent.

Armitage *et al.* discloses that bis-PNA is effective at forming strand invasion complexes with duplex DNA.

Applicants respectfully repeat that, for a rejection under 35 U.S.C. § 103 to be properly founded, each and every element of the claim must be disclosed in the combination of cited references. The deficiencies of Vary and Kai *et al.* are not satisfied by Armitage *et al.* for at least the following reasons. Vary, Kai *et al.* and Armitage *et al.*, individually or combined, **fail** to disclose the use of bis-PNA to detect triplex structures resulting from the binding of amplified target sequence to PNA, as required in the method of Claim 2. One of ordinary skill in the art would therefore lack the motivation to make or use the claimed method in view of the cited art. For at least the foregoing reasons, withdrawal of the rejection is respectfully requested.

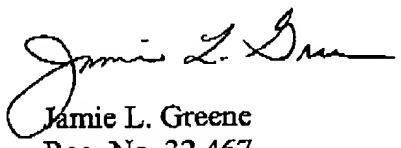
Conclusion

In light of the amendments and the above remarks, applicants are of the opinion that the Office Action has been completely responded to and that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6500 is respectfully requested.

No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies that may be required, or credit any overpayment, to Deposit Account Number 11-0855.

Respectfully submitted,



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